CDC Influenza Division Technical Key Points
February 16, 2018

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Summary Key Points

- Seasonal influenza activity in the United States remained high in this week's FluView report.
- This week, 48 states are still reporting widespread geographic influenza activity. Oregon is reporting regional activity. Hawaii is now reporting local activity (down from regional last week).
- The proportion of people seeing their health care provider for influenza-like-illness (ILI) remained stable.
    - Note: With backfilled ILI data, ILI for week 5 is 7.5% (down from 7.7% reported last week), and remains at 7.5% for week 6.
- These are the highest levels of ILI recorded since the 2009 H1N1 pandemic, which peaked at 7.7% ILI.
- Forty-three states, the District of Columbia, New York City and Puerto Rico experienced high ILI activity. (This is the same as was reported last week).
- This is the 12th week that ILI has been at or above the national baseline.
- By this measure, the past five seasons have averaged 16 weeks, with the longest season lasting 20 weeks.
- It's likely there will be significant flu activity for many weeks to come.
- Flu activity indicators are notable for the sheer volume and intensity of flu that is occurring in most of the country at the same time.
- While H3N2 viruses continue to be predominant this season, the overall proportion of influenza A viruses is declining and the proportion of influenza B viruses is increasing. H1N1 viruses are also increasing in number though not as much as B viruses.
- There is usually co-circulation of influenza viruses during any one season and it's not uncommon for there to be second waves of influenza B activity during an influenza season also.

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- In past seasons similar to this one, an estimated 34 million Americans have gotten sick with flu.
- The cumulative hospitalization rate (for week 6) is 67.9/100,000, which is higher than was seen for this same week during the 2014-2015 season (52.9) and is higher than the end-of-season cumulative rate of 64.2/100,000.
- 2014-2015 season was a high severity, H3N2-predominant season.
- The highest hospitalization rate is among people 65 and older at 294.9/100,000. This rate is higher than what was reported for the same week of 2014-2015 (262.1/100,000) and approaching the final cumulative rate of 308.8 per 100,000 that season.
- The next highest rate is among people 50 to 64 years of age. At 72.8/100,000, this rate is higher than both the week 6 report of 41.7 and the cumulative end-of-season rate of 53.4/100,000 for the 2014-2015 season.
- The next highest rate is among children 0-4 years. At 47.1/100,000, their hospitalization rate is slightly higher than the 45.3/100,000 rate reported during week 6 of 2014-2015 but still lower than the cumulative end of season rate of 57.3/100,000.
- So for people 50 years and older, this is turning out to be a more severe season than 2014-2015 in terms of hospitalizations. We still need to wait to see whether it is also more severe for children.
- It seems that the rate of increase in hospitalizations is slowing.
- However, it is possible that the number of flu hospitalizations may exceed 710,000, which is the high end of the estimated number of hospitalizations that have occurred in the United States since 2010.
- The proportion of deaths attributed to pneumonia and influenza (P & I) is down slightly this week to 9.8% but remains above the epidemic threshold, which means that more deaths are occurring due to pneumonia and influenza that would be expected at this time.
- P & I has been above the epidemic threshold for 6 weeks.
- An additional 22 flu-related pediatric deaths were reported this week, bringing the total number of flu-related pediatric deaths reported to CDC so far to 84.
- This is the highest number of pediatric deaths ever reported during a single week of a regular flu season since pediatric deaths became nationally notifiable in 2004.
- Previously, the highest number of pediatric deaths reported during one week was 19 deaths during the 2014-2015 season.
- Early, interim influenza vaccine effectiveness (VE) for this season were published on Thursday.
- Overall VE was 36%. That means a vaccinated person’s risk of having to go to the doctor because of flu was reduced by more than one-third.
- Effectiveness was 25% against H3N2, 67% against H1N1 and 42% against influenza B viruses.
- These findings are similar to what has been observed in the past.

    - A study that looked at a number of VE estimates from 2004-2015 found average VE of 33% (CI = 26%–39%) against H3N2 viruses, compared with 61% (CI = 57%–65%) against H1N1 and 54% (CI = 46%–61%) against influenza B viruses.
- It is noteworthy that VE against H3N2 among children 6 months to 8 years old was 51%.
- The relatively lower vaccine effectiveness seen against H3N2 viruses may, in part, be caused by egg-adapted changes introduced when H3N2 viruses are optimized for growth in eggs, which is required for the egg-based production used to produce most U.S. flu vaccines.
- Other factors may be playing a role in reduced VE against H3N2 this season, including host factors. (See U.S. VE key points).
- CDC recommends a 3-pronged strategy to fight flu. 1. Take time to get a flu vaccine. 2, Take everyday preventive actions, including staying away from sick people, and 3, Take antiviral drugs if your doctor prescribes them.
- As long as flu viruses are circulating, vaccination should continue throughout the flu season, even in January.
- There are many reasons to get a flu vaccine.
    1. While flu vaccine can vary in how well it works, it is the best way to prevent flu illness and serious flu complications, including those that can result in hospitalization.
    2. We cannot know which viruses will circulate over the season and which virus will predominate. Flu vaccine protects against three or four different flu viruses, depending on which vaccine you get.
    3. A 2017 study was the first of its kind to show that flu vaccination can significantly reduce a child's risk of dying from influenza.
    4. Getting vaccinated yourself protects people around you, including those who are more vulnerable to serious flu illness, like babies and young children, older people, and people with certain chronic health conditions.
    5. While flu vaccine is not perfect and some people who get vaccinated may still get flu, there is some data to suggest that flu vaccination may make illness milder.
- While flu vaccine is the best way to prevent flu, influenza antiviral drugs are a second line of defense that can be used to treat flu illness.
- Most people who are otherwise healthy and get the flu do not need to be treated with antiviral drugs, but some people are more likely to get very sick, especially the very young, the very old, pregnant women, and those with medical conditions that put them at high risk for developing severe infection.
- CDC recommends prompt treatment with flu antiviral drugs for people who are very sick with flu symptoms or people who are at high risk of developing serious flu complications when they get flu symptoms.

- The volume of flu the country is experiencing right now has led to spot shortages of flu vaccine, antiviral drugs and even tests to quickly diagnose flu.
- People may need to be persistent to locate vaccine, antiviral drugs to fill a prescription.

Key Flu Indicators

Influenza activity remains elevated according to the latest FluView report. All U.S. states but Hawaii and Oregon continue to report widespread flu activity and 43 states plus New York City, the District of Columbia and Puerto Rico continue to report high influenza-like illness (ILI) activity. The overall hospitalization rate is higher than the overall hospitalization rate reported for the same week of 2014-2015; a high severity, H3N2-predominant season. CDC also is reporting an additional 22 flu-related pediatric deaths during week 6, bringing the total number of flu-related pediatric deaths reported this season to 84. Among reported pediatric flu deaths this season, only 26% of children eligible for vaccination had received any flu vaccine this season before they got sick. Flu activity is likely to remain elevated for several more weeks.

CDC continues to recommend influenza vaccination for all persons 6 months of age and older as flu viruses are likely to continue circulating for weeks and there is an increasing proportion of influenza B and H1N1 viruses being detected. Early estimates show that flu vaccine has reduced risk of having to go to the doctor due to flu by 36% overall so far this season and that flu vaccine is offering substantial protection against H1N1 flu as well as moderate protection against flu B viruses. In addition, in the context of widespread influenza activity, CDC is reminding clinicians and the public about the importance of prompt treatment with antiviral medications in people who are severely ill and people who are at high risk of serious flu complications who develop flu symptoms. Below is a summary of the key flu indicators for the week ending February 10, 2018 (week 6):

- **Influenza-like Illness Surveillance:** For the week ending February 10, the proportion of people seeing their health care provider for influenza-like illness (ILI) was 7.5%, which is above the national baseline of 2.2%. Last week (week 5), ILI was reported to have reached 7.7%, the same as the peak of the 2009 H1N1 pandemic, however, additional data submitted for week 5 subsequently has resulted in the week 5 ILI being recalculated at 7.5%. All 10 regions reported a proportion of outpatient visits for ILI at or above their region-specific baseline levels. ILI has been at or above the national baseline for 12 weeks so far this season. Over the past five seasons, ILI has remained at or above baseline for 16 weeks on average.
    - Additional ILINet data, including national, regional, and select state-level data for the current and previous seasons, can be found at http://gis.cdc.gov/grasp/fluview/fluportaldashboard.html.

- **Influenza-like Illness State Activity Indicator Map:** New York City, the District of Columbia, Puerto Rico and 43 states experienced high ILI activity (Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Vermont, Virginia, West Virginia, Wisconsin, and Wyoming). Two states (North Dakota and Utah) experienced moderate ILI activity. Three states experienced low ILI activity (Hawaii, Idaho, and Washington). Two states experienced minimal ILI activity (Maine and Montana).

    - Additional data, including data for previous seasons, can be found at https://gis.cdc.gov/grasp/fluview/main.html

- **Geographic Spread of Influenza Viruses:** Widespread influenza activity was reported by Puerto Rico and 48 states (Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, and Wyoming). Regional influenza activity was reported by Oregon. Local influenza activity was reported by the District of Columbia, Guam and one state (Hawaii). No flu activity was reported by the U.S. Virgin Islands. Geographic spread data show how many areas within a state or territory are seeing flu activity.

    - Additional data are available at: https://gis.cdc.gov/grasp/fluview/FluView8.html.

- **Flu-Associated Hospitalizations:** Since October 1, 2017, 19,398 laboratory-confirmed influenza-associated hospitalizations have been reported through the Influenza Hospitalization Network (FluSurv-NET), a population-based surveillance network for laboratory-confirmed influenza-associated hospitalizations. This translates to a cumulative overall rate of 67.9 hospitalizations per 100,000 people in the United States.

    - The highest hospitalization rate is among people 65 years and older (294.9 per 100,000), followed by adults aged 50-64 years (72.8 per 100,000), and younger children aged 0-4 years (47.1 per 100,000). During most seasons, adults 65 years and older have the highest hospitalization rates, followed by children 0-4 years.

- During the 2014-2015 season, the cumulative overall hospitalization rate reported during week 6 was 48.6 per 100,000. During that same week, hospitalization rates for people 65 years and older were 242.2 per 100,000. Hospitalization rates for younger children 0-4 years were 43.4 per 100,000.
- Hospitalization data are collected from 13 states and represent approximately 9% of the total U.S. population. The number of hospitalizations reported does not reflect the actual total number of influenza-associated hospitalizations in the United States. Additional data, including hospitalization rates during other influenza seasons, can be found at http://gis.cdc.gov/GRASP/Fluview/FluHospRates.html and http://gis.cdc.gov/grasp/fluview/FluHospChars.html.

- **Mortality Surveillance:**
  - The proportion of deaths attributed to pneumonia and influenza (P&I) is high again at 9.8% for the week ending January 27, 2018 (week 4). This percentage is above the epidemic threshold of 7.3% for week 4 in the National Center for Health Statistics (NCHS) Mortality Surveillance System.
  - Region and state-specific data are available at https://gis.cdc.gov/grasp/fluview/mortality.html.

- **Pediatric Deaths**
  - 22 influenza-associated pediatric deaths were reported to CDC during week 6.
    - Four deaths were associated with an influenza A(H3) virus and occurred during weeks 2, 4, and 5 (the weeks ending January 13, January 27, and February 3, 2018, respectively). Five deaths were associated with an influenza A(H1N1)pdm09 virus and occurred during weeks 52, 5, and 6 (the weeks ending December 30, 2017, February 3, and February 10, 2018, respectively). Eight deaths were associated with an influenza A virus for which no subtyping was performed and occurred during weeks 51, 2, 3, 5, and 6 (the weeks ending December 23, 2017, January 13, January 20, February 3, and February 10, 2018, respectively). Five deaths were associated with an influenza B virus and occurred during weeks 2, 5 and 6 (the weeks ending January 13, February 3, and February 10, 2018, respectively).
    - One death that was reported earlier this season was reclassified by the reporting jurisdiction.
  - A total of 84 influenza-associated pediatric deaths for the 2017-2018 flu season have been reported to CDC.
    - Additional information on pediatric deaths is available on FluView Interactive at: https://gis.cdc.gov/GRASP/Fluview/PedFluDeath.html.

- **Laboratory Data:**
  - Nationally, the percentage of respiratory specimens testing positive for influenza viruses in clinical laboratories during the week ending February 10 was 26.5%.
  - Regionally, the three-week average percent of specimens testing positive for influenza in clinical laboratories ranged from 15.0% to 31.4%.
  - During the week ending February 10, of the 17,040 (26.5%) influenza-positive tests reported to CDC by clinical laboratories, 10,837 (63.6%) were influenza A viruses and 6,203 (36.4%) were influenza B viruses.
  - The most frequently identified influenza virus subtype reported by public health laboratories was influenza A(H3N2) virus.
  - During the week ending February 10, 1,109 (66.2%) of the 1,676 influenza-positive tests reported to CDC by public health laboratories were influenza A viruses and 567 (33.8%) were influenza B viruses. Of the 1,071 influenza A viruses that were subtyped, 870 (81.2%) were H3N2 viruses and 201 (18.8%) were (H1N1)pdm09 viruses.
  - The majority of the influenza viruses collected from the United States during October 1, 2017 through February 10, 2018 were characterized antigenically and genetically as being similar to the cell-grown reference viruses representing the 2017–18 Northern Hemisphere influenza vaccine viruses.
  - Since October 1, 2017, CDC has tested 431 influenza A(H1N1)pdm09, 962 influenza A(H3N2), and 418 influenza B viruses for resistance to antiviral medications (i.e. oseltamivir, zanamivir, or peramivir). While the majority of the tested viruses showed susceptibility to the antiviral drugs, four (0.9%) H1N1pdm09 viruses were resistant to both oseltamivir and peramivir, but was sensitive to zanamivir.

FluView (http://www.cdc.gov/flu/weekly/fluactivitysurv.htm) is available – and past issues are archived (http://www.cdc.gov/flu/weekly/pastreports.htm) – on the CDC website.

Note: Delays in reporting may mean that data changes over time. The most up to date data for all weeks during the 2017-2018 season can be found on the current FluView(http://www.cdc.gov/flu/weekly/) and FluView Interactive (https://www.cdc.gov/flu/weekly/fluviewinteractive.htm).

Pediatric Deaths

- Twenty-two influenza-associated pediatric deaths were reported to CDC during week 6 of the 2017-2018 season.
- Four deaths were associated with an influenza A(H3) virus and occurred during weeks 2, 4, and 5 (the weeks ending January 13, January 27, and February 3, 2018, respectively). Five deaths were associated with an influenza A(H1N1)pdm09 virus and occurred during weeks 52, 5, and 6 (the weeks ending December 30,

2017, February 3, and February 10, 2018, respectively). Eight deaths were associated with an influenza A virus for which no subtyping was performed and occurred during weeks 51, 2, 3, 5, and 6 (the weeks ending December 23, 2017, January 13, January 20, February 3, and February 10, 2018, respectively). Five deaths were associated with an influenza B virus and occurred during weeks 2, 5 and 6 (the weeks ending January 13, February 3, and February 10, 2018, respectively). A total of 84 influenza-associated pediatric deaths have been reported for the 2017-2018 season.

- Since 2004, when pediatric deaths associated with influenza infection became nationally notifiable, the number of deaths reported to CDC each year has ranged from 37 (2011-2012 season) to 171 deaths (2012-2013 season).
- Last season, 2016-2017, 110 influenza-associated pediatric deaths were reported to CDC.
- During past seasons, approximately 80% of flu-associated deaths in children have occurred in children who were not vaccinated. This proportion is similar for 2017-2018 season (74% as of week 5).
- Since the 2010-2011, between 43.8% to 59% of pediatric deaths occurred in children who were otherwise healthy and didn't have an underlying medical condition.
- Because of confidentiality issues, CDC does not discuss or give details on individuals.
- These deaths are a somber reminder of the danger flu poses to children.
- The single best way to protect against seasonal flu and its potentially severe consequences in children is to get a seasonal flu vaccine each year.
- Vaccination is important for children younger than 5 years. It is especially important for those younger than 2 years and children of any age with a long-term health condition like asthma, diabetes and heart disease and neurological and neurodevelopmental diseases. These children are at higher risk of serious flu complications if they get the flu.
- Yearly vaccination also is especially important for people in contact with high risk children in order to protect the child (or children) in their lives from the flu. In particular, children younger than 6 months are too young to be vaccinated themselves but are at high risk of flu complications if they get sick so the people around them should get vaccinated to protect the infant.
- Some children 6 months through 8 years of age require 2 doses of influenza vaccine. Children in this age group who are getting vaccinated for the first time will need two doses. Some children who have received influenza vaccine previously also will need two doses this season. A health care provider should be consulted to determine whether two doses are recommended for a child.
- Flu-associated deaths in children younger than 18 years old should be reported through the Influenza-Associated Pediatric Mortality Surveillance System. The number of flu-associated deaths among children reported during the 2017-2018 flu

season will be updated each week and can be found at www.cdc.gov/flu/weekly/ and https://gis.cdc.gov/GRASP/Fluview/PedFluDeath.html.

U.S. Flu Vaccine Effectiveness Estimates

Topline Messages

- On February 15, CDC published a Morbidity and Mortality Weekly Report (MMWR) entitled "Interim Estimates of 2017-18 Seasonal Influenza Vaccine Effectiveness – United States, February 2018." This report is available online at https://www.cdc.gov/mmwr/index.html .
- During each flu season since 2004-2005, CDC has estimated the effectiveness of seasonal flu vaccines to prevent laboratory-confirmed flu illness resulting in a doctor's visit.*

  *Clinically what is being measured is laboratory confirmed influenza associated with medically attended acute respiratory illness (ARI).

- This report uses data from 4,562 children and adults enrolled in the U.S. Influenza Vaccine Effectiveness Network (U.S. Flu VE Network) during November 2, 2017 – February 3, 2018.
- During this period, overall adjusted vaccine effectiveness (VE) against influenza A and B virus infection was **36%** (95% CI: 27% to 44%).
- This means that CDC's early 2017-2018 estimates show the flu vaccine has performed similarly to what CDC expected at the beginning of the season with A(H3N2) viruses driving the majority of flu activity. Overall, the seasonal flu vaccine has reduced the risk of getting sick and having to go to the doctor from flu by about one third.
- Influenza A(H3N2) viruses were responsible for most (69%) of the flu infections reported in this study, and as expected, VE was lower against influenza A(H3N2) viruses.
- VE was **25%** (95% CI: 13%–36%) against illness caused specifically by influenza A(H3N2) viruses.
- Of note: VE was much higher in children 6 months through 8 years of age: overall VE against influenza A and B viruses was **59%** (95% CI: 44%–69%) in this age group.
- Children in this age group also had higher VE specifically against A(H3N2). VE against A(H3N2) viruses was 51% (95% CI: 29%—66%) in children 6 months through 8 years of age. This means the risk for A(H3N2) illness that required a doctor's visit was reduced by more than half among this group of vaccinated children.
- VE against other flu viruses, including against influenza A(H1N1) and influenza B viruses, also was higher than against A(H3N2).
  - VE was **67%** (CI:54%–76%) against influenza A(H1N1)pdm09 viruses

  - VE was **42%** (CI: 25%–56%) against influenza B viruses, providing a moderate level of protection.

- These interim VE estimates reflect the ongoing challenges with creating effective flu vaccines against influenza A(H3N2) viruses. (H3N2 viruses have proven problematic since the 2011–12 season.)
- The interim estimate of 25% VE against A(H3N2) viruses this season shows that seasonal flu vaccines are providing some protection, in contrast to recently reported, non-significant interim estimates of 17% from Canada and 10% from Australia.
- These results also are similar to the final U.S. VE estimates of 32% against A(H3N2) viruses reported last season (2016-2017).
- However, there is room for improvement.
- There are many possible reasons for lower effectiveness against H3N2 viruses, and it's important to get more data to help develop better flu vaccines.
- Several hypotheses for why flu vaccines provide less benefit against H3N2 viruses could include the following:
  - Host factors, such as how a person's unique immune system responds to vaccination or previous flu infections.
    - Note: some existing science suggests that the flu viruses people are exposed to early in life will affect the way their immune systems respond to flu infection or vaccination later in life – a process called "imprinting" or "original antigenic sin."
  - Another factor could be the unique characteristics of circulating H3N2 viruses and changes that occur in H3N2 viruses over time.
  - And lastly, the egg-adapted changes that occur with greater frequency in H3N2 viruses when they are grown in eggs as part of the flu vaccine manufacturing process. Note: A(H3N2) viruses are particularly difficult to grow in eggs.
- While these points represent factors that public health scientists and officials must study and better understand in the future, these early VE estimates also underscore the need for ongoing influenza prevention and treatment measures now.
- CDC continues to recommend flu vaccination because the flu vaccine can still prevent some infections with flu viruses that are expected to continue circulating for several weeks.
  - Vaccine effectiveness point estimates for influenza B and A (H1N1) indicate that 2017-2018 flu vaccines will reduce people's risk of flu illness associated with influenza B or A(H1N1) viruses that results in a doctor's visit by 42% to 67%.
  - Also, even with vaccine effectiveness of 25% against H3N2 viruses, flu vaccination will still prevent a substantial amount of illness due to this virus.
  - Flu vaccination has prevented thousands of hospitalizations during previous seasons when A(H3N2) viruses were predominant, including during the

2014–15 season when interim VE estimates were similar to those reported here.

- In the United States, annual vaccination against seasonal flu is recommended for all people 6 months of age and older.
- In addition, appropriate use of flu antiviral medications for treatment of severely ill people or people at high risk for complications from the flu who develop flu symptoms is important, especially among older adults, who currently have the highest hospitalization rates.
- The VE estimates being reported today are interim estimates for the 2017-2018 season, and the final VE estimates will be published after the season is over. The final season VE estimates may differ from these interim estimates, and based on previous end of season estimates, they may be a little lower than the interim estimates.
- CDC will continue to monitor vaccine effectiveness through the rest of the season. Yearly monitoring of vaccine effectiveness is critical to identifying vaccine issues that need to be understood and corrected.

Methods

- At five study sites, patients 6 months of age and older seeking outpatient medical care for ARI with cough within 7 days of illness onset were enrolled. The five study sites of the U.S. Flu VE Network are located in the following states:
    - Wisconsin,
    - Michigan,
    - Washington
    - Pennsylvania, and
    - Texas.
- Participants were interviewed to collect demographic data, information on general and current health status, and symptoms, and 2017-2018 vaccination status.
    - (Note: a limitation of this current data is that vaccination status included self-report at four of five sites. Self-reporting can bias results towards higher vaccination rates.)
- Nasal and oropharyngeal swabs (or nasal swabs) were collected to obtain respiratory specimens.
- Specimens were tested at U.S. Flu VE Network laboratories using CDC's rRT-PCR protocol.
- VE against all influenza virus types combined and against viruses by type/subtype were estimated as 100% x (1 – odds ratio).
- Estimates were adjusted for study site, age group, sex, race/ethnicity, self-rated general health, number of days from illness onset to enrollment, and week of illness.

- Interim VE estimates for the 2017-18 season were based on patients enrolled through February 3, 2018.

Results

- Among the 4,562 children and adults with ARI enrolled at the five study sites from November 2, 2017 through February 3, 2018, a total of 1,712 (38%) tested positive for influenza by rRT-PCR, including 1,392 (81%) influenza A viruses and 323 (19%) influenza B viruses.
- Among 1,340 subtyped influenza A viruses, 1,143 (85%) were A/(H3N2) viruses and 208 (16%) were A(H1N1)pdm09 viruses.
- Most (98%) of influenza B viruses belonged to the B/Yamagata lineage.
- The proportion of patients with influenza differed by study site, sex, age group, race/ethnicity, self-rated health status, and interval from illness onset to enrollment.
- The percentage of patients who were vaccinated ranged from 45% to 59% among study sites and differed by sex, age group, race/ethnicity, and self-rated health status.
- Among ARI patient participants, 43% of those with influenza had received the 2017-2018 seasonal influenza vaccine, compared with 53% of influenza –negative participants.
- VE During this period, overall adjusted vaccine effectiveness (VE) against influenza A and B virus infection associated with medically attended ARI was **36%** (95% CI: 27% to 44%).
    - Most (69%) of influenza infections were caused by influenza A(H3N2) viruses.
    - VE was estimated to be **25%** (95% CI: 13%–36%) against illness caused by influenza A(H3N2) viruses
    - Of note: statistically significant protection against medically attended influenza was found among children 6 months through 8 years of age: VE was 59% (95% CI: 44%–69%).
    - VE was estimated to be **67%** (CI:54%–76%) against A(H1N1)pdm09 viruses
    - VE was estimated to be **42%** (CI: 25%–56%) against influenza B viruses.
- As of February 3, 2018, a total of 257 influenza A(H3N2) viruses from U.S. Flu VE Network participants had been characterized by CDC.
    - 240 (93%) belonged to either genetic group 3C.2a (226 viruses) or to the related subgroup 3C.2a1 (14), whereas 17 (7%) belonged to group 3C.3a.
    - Genetic group 3C.2a includes the A/Hong Kong/4801/2014 reference virus representing the A(H3N2) component of the 2017-2018 Northern Hemisphere influenza vaccines.

CDC Influenza Division Key Points
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Background

- Each season, CDC studies how well flu vaccines work by collecting data through the U.S. VE network of five sites across the United States.
- Flu vaccine effectiveness can vary each year based on a number of factors, including the match between vaccine viruses and circulating viruses, what viruses are circulating, and the age and immune factors of the person being vaccinated.
- CDC will continue to publish influenza laboratory and disease surveillance data weekly in FluView.
- Updated VE estimates will be provided as warranted and final VE estimates will be published after the season ends. Final season VE estimates may differ from the interim estimates, and may be a little lower than the interim estimates.

Vaccine Effectiveness, General

- While vaccine effectiveness can vary, a study that pooled influenza vaccine effectiveness estimates from 2007 to 2015 by virus type and subtype found that:
    - Multi-year pooled vaccine effectiveness against influenza B viruses was 54%;
    - Multi-year pooled vaccine effectiveness against influenza A(H1N1)pdm09 viruses was 61%;
    - Multi-year pooled vaccine effectiveness against H3N2 viruses was 33%.
        - Belongia EA, Simpson, MD, King JF, Sundaran ME, Kelley NS, Osterholm MT, McLean HQ. Variable influenza vaccine effectiveness by subtype: a systematic review and meta-analysis of test-negative design studies. Lancet Infect Dis. 2016; 16(8):942-51.
- It is important to note that during seasons when the majority of circulating viruses are very different from a vaccine virus, vaccine effectiveness can be further reduced.
- Two types of genetic changes can impact the similarity between a vaccine virus and circulating seasonal viruses.
    1. Influenza viruses constantly undergo small genetic changes. These genetic changes can sometimes result in antigenic changes. This is called **"antigenic drift."** (Circulating viruses "drift" away from what is included in the vaccine.)
        - For more information on antigenic changes, see CDC's Antigenic Characterization page at https://www.cdc.gov/flu/professionals/laboratory/antigenic.htm.
    2. Another type of change that can happen is that genetic changes occur when influenza viruses are grown in eggs, which is required for most U.S. flu vaccines.
        - These genetic changes (called **"egg-adapted"** changes) may have antigenic (or immunogenic) implications that may impact how well the vaccine works.
        - Egg-adapted changes that are associated with antigenic changes occur more often in H3N2 viruses.

- The lower vaccine effectiveness seen against H3N2 viruses during seasons when no antigenic drift has occurred may, in part, be caused by egg-adapted changes.
- Most U.S. flu vaccines are produced using egg-based technology.
- There are two flu vaccines in the United States that are not grown in eggs: recombinant influenza vaccine (Flublok) and cell-grown influenza vaccine (Flucelvax).
    - Recombinant vaccine is made by growing a certain protein from a naturally occurring ("wild type") recommended vaccine virus in insect cells.
    - This season, Flucelvax is being made using a cell-grown H3N2 candidate vaccine virus for the first time.
    - Previously Flucelvax had been produced using cell-based technology but with candidate vaccine viruses isolated in eggs per FDA regulatory requirements.
    - On August 31, 2016, FDA approved the use of cell-isolated candidate vaccine viruses in the production of Flucelvax, the only licensed cell-based flu vaccine in the United States.
- For recombinant and cell-grown vaccines, the H3N2 components are genetically more similar to circulating H3N2 viruses than the egg-adapted viruses recommended for egg-based manufacturing.
- At this time there is insufficient data to determine whether cell-based or recombinant vaccine are more effective than egg-based vaccine.
- Additional data is needed (including vaccine effectiveness data) before policy decisions on this topic could be considered.

Flu & Sepsis

- Flu infection can be associated with sepsis, even in otherwise healthy people, and that is a life-threatening condition.
- CDC has received reports from some state health departments of flu deaths associated with sepsis this season.
- A recent CDC study found that 30% of pediatric death reports included sepsis listed as a complication.
- More information about sepsis can be found at https://www.cdc.gov/sepsis/index.html

Vaccine Availability

- Manufacturers report having shipped more than 154.7 million doses of flu vaccine as of February 9, 2018.
- The total projected supply of vaccine in the United States this season is between 151 million and 166 million doses of flu vaccine. About 119 million doses will be quadrivalent vaccine.

CDC Influenza Division Key Points
February 16, 2018

For Patients:
CDC continues to recommend flu vaccination as the first line of defense against the flu. While some individual providers may be running low on flu vaccine at this point in the season, flu vaccine is available from a variety of providers throughout the country. Call your doctor, or use the flu vaccine finder to find where vaccine is available in your community.

For Providers:
Flu vaccine is available, but providers may not be able to get every brand and/or presentation, and they may have to purchase from a different source. Providers interested in purchasing vaccine should check the influenza vaccine tracking availability system (IVATS) available at: https://www.izsummitpartners.org/ivats/.

Antiviral Supply Update

- CDC is in regular contact with influenza antiviral manufacturers regarding supply and other issues.
- Some manufacturers are reporting delays in filling orders and CDC is aware of spot shortages of antiviral drugs specifically for oseltamivir suspension and generic oseltamivir capsules in some places experiencing high influenza activity.
- CDC is working with manufacturers, distributors, pharmacies, and pharmacy benefit managers to understand and address existing gaps in the market, including increasing access to brand name influenza antiviral medications, particularly for oseltamivir, in areas where there may be spot shortages of the generic version of the drug.
- In response to high influenza activity this season and the high volume of influenza antiviral prescriptions dispensed, Genentech (i.e., the manufacturer of Tamiflu®, the brand name version of oseltamivir) has taken additional actions to increase patient access to product.
    - See Press release: https://www.gene.com/media/statements/ps_020518.
- Additionally, major pharmacy benefit managers, including Express Scripts and OptumRX, have made Tamiflu® capsules and suspension preferred on their formularies (single source brand/preferred brand). A formulary is a list of drugs covered by an insurance company. So this move means that some insurance companies will now cover brand name oseltamivir (i.e., Tamiflu®), and it will allow for the drug to be covered at the lowest cost for a brand name drug (as determined by individual insurance companies).
- In addition, ***some*** insurance company prescription plans are allowing the brand name product to be processed as generic, if the generic version of the drug is not

available. This means that they will cover Tamiflu® for the same copay as generic brands of oseltamivir, if the generic version is not available.

- People seeking influenza antiviral medications, such as oseltamivir, are encouraged to check with their pharmacy or insurance company if they have additional questions on individual drug coverage.
- Visit CDC's antiviral supply page for the latest updates at https://www.cdc.gov/flu/professionals/antivirals/supply.htm.

Additional Considerations:

- Pharmacists should consider compounding oseltamivir suspension by using oseltamivir 75 mg capsules, if suspension is not readily available for patients that need it.
- Pharmacies and others attempting to make bulk purchases of influenza antiviral drugs may need to call more than one distributor or manufacturer to locate medications available for purchase in the short term. CDC has updated its antiviral drug supply web page with manufacturer information for inquires related to antiviral purchases/availability.
- Individual patients seeking to fill an influenza antiviral prescription may want to call ahead to make sure their pharmacy has product on the shelf to fill their prescription. It may be necessary to call more than one pharmacy to locate these medications.
- Additional discounts may be available through some pharmaceutical providers.
    - See example news story: https://www.prnewswire.com/news-releases/inside-rx-provides-savings-on-influenza-medications-300593061.html.
- Antiviral drugs work better the earlier you begin taking them so prompt action is important.
- For people who have flu and are at high risk of serious flu complications, treatment with an antiviral drug can mean the difference between having a milder illness and having a very serious illness that could result in a hospital stay.

Supply of Flu Tests & Testing Guidance

- CDC has received reports of spot shortages of some influenza tests, including Rapid Influenza Diagnostic Tests (RIDTs) and Reverse Transcription-Polymerase Chain Reaction (RT-PCR).
- These reports coincide with an ongoing intense and widespread seasonal influenza epidemic, during which spot shortage of flu vaccines and influenza antiviral medications also have been observed.

  - RIDTs are tests that can identify the presence of influenza A and B viral nucleoprotein antigens in respiratory specimens, and display the result.
  - While RIDTs can be important for diagnosis and treatment, how well they work can vary dramatically based on a number of factors.
  - Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and other molecular assays can identify the presence of influenza viral RNA in respiratory specimens.
    - These test are generally much more reliable and are recommended by CDC for use on hospitalized patients.
- According to CDC guidance, testing is not needed for all patients with signs and symptoms of influenza to make antiviral treatment decisions.
- Once influenza activity has been documented in the community or geographic area, a clinical diagnosis of influenza can be made for outpatients with signs and symptoms consistent with suspected influenza, especially during periods of peak influenza activity in the community.
- Guidance for Clinicians on the Use of RT-PCR and Other Molecular Assays for Diagnosis of Influenza Virus Infection is available at https://www.cdc.gov/flu/professionals/diagnosis/molecular-assays.htm .
- Guidance on the use of RIDTs is available at https://www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm .

Influenza Treatment: Antiviral Medications

- Antiviral drugs are prescription medicines (pills, liquid or an inhaled powder) and are not available over the counter.
- Influenza antiviral drugs are the only drugs approved to treat influenza infection.
- Antiviral drugs are different from antibiotics. Antiviral drugs fight viruses (like flu viruses) in your body; antibiotics fight infections in your body that are caused by bacteria.
- Antiviral drugs can make flu illness milder and shorten the time you are sick.
- There also are data showing that antiviral drugs may prevent serious flu complications such as pneumonia and hospitalizations in outpatients, and reduce mortality and length of stay in hospitalized patients.
  - For example, in 2015, a CDC study found that early treatment of flu-hospitalized people 65 and older with flu antiviral medications cut the duration of their hospital stay and reduced their risk of needing extended care after discharge.
  - This study entitled "Impact of Prompt Influenza Antiviral Treatment on Extended Care Needs After Influenza Hospitalization Among Community-Dwelling Older Adults" by Sandra Chaves et al. is available from the Clinical Infectious Diseases journal website at http://cid.oxfordjournals.org/content/early/2015/09/01/cid.civ733 .
- Antiviral drugs work best when started within two days of symptoms first appearing, but there are data to suggest they can still be beneficial in very ill

patients even up to five days after getting sick. This would be especially important for a person who is at high risk of serious flu complications and who is very sick.

- Three FDA-approved influenza antiviral drugs are recommended for use in the United States during the 2017-2018 influenza season: oseltamivir (Tamiflu® and generic formulations), zanamivir (Relenza®), and peramivir (Rapivab®). Generic formulations of oseltamivir became available commercially last season.
- Antiviral drugs are not a substitute for getting a flu vaccine. The flu vaccine is the best way modern medicine currently has to prevent this potentially serious disease.
- See Influenza Antiviral Medications: Summary for Clinicians on the CDC web site for additional information.

Antiviral Side Effects Summary

- With all medications there are reported side effects:

Oral oseltamivir

- This medication can be used for treatment of people of all ages
- Adverse reactions to oseltamivir include nausea, vomiting and headache.
- There have also been some post-marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events.

Inhaled zanamivir

- This drug can be used for treatment in those 7 years and older; however it isn't recommended for use in people with underlying respiratory diseases (e.g., asthma, COPD), nor is it recommended for patients hospitalized with influenza
- Zanamivir can be used for chemo-prophylaxis of those 5 years and older; however they shouldn't use it if they have they have underlying respiratory diseases (e.g., asthma, COPD)
- Allergic reactions have been reported to throat or facial swelling and a skin rash.
- Some adverse reactions to zanamivir include bronchospasm, especially in the setting of underlying airways disease; sinusitis, dizziness, and ear, nose and throat infections.
- There were some post-marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events

Intravenous peramivir

- This drug can be used for treatment of those 2 years and older
- Some adverse reactions to peramivir include diarrhea.
- There were some post-marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events

For more information on safety, effectiveness and dosing for oral oseltamivir, inhaled zanamivir, and intravenous peramivir, visit the Food and Drugs Administration (FDA)

website https://www.fda.gov/Drugs/DrugSafety/ and/or consult the product package inserts.

Communications Activities

- On December 27, 2017, CDC issued a Health Advisory (https://emergency.cdc.gov/han/han00409.asp) through the Health Alert Network, providing notice about 1) increased influenza A(H3N2) activity and its clinical implications, 2) a summary of influenza antiviral drug treatment recommendations, 3) an update about approved treatment drugs and supply this season, and 4) background information for patients about influenza treatment.
- The transcript for a January 12, 2018, is available at https://www.cdc.gov/media/releases/2018/t0112-widespread-flu-activity.html.
- The video of a January 16, 2017, Public Health Grand Rounds on the influenza is available at https://www.cdc.gov/cdcgrandrounds/archives/2018/January2018.htm.
- A transcript for a telebriefing held on January 26, 2018 is available at https://www.cdc.gov/media/releases/2018/t0126-flu-update-activity.html.
- On Friday, February 2, 2018, a telebriefing was held. A transcript will be available at https://www.cdc.gov/media/releases/2018/t0202-flu-update-activity.html.
- On Friday, February 9, 2018, a telebriefing was held. A transcript will be available at https://www.cdc.gov/media/releases/2018/t0209-flu-update-activity.html.
- On Monday, February 12 a study on flu-related pediatric deaths appeared in the journal Pediatrics. The study: "Influenza-Associated Pediatric Deaths in the United States, 2010–2016" is available at http://pediatrics.aappublications.org/content/early/2018/02/09/peds.2017-2918.
- On Thursday, February 15, HHS Secretary Alex Azar, joined by Acting CDC Director Anne Schuchat and others, held a press briefing to update the American public on the current state of influenza activity in the United States. Video of the briefing is available on the HHS YouTube page at https://www.youtube.com/watch?v=OeNyLGlNryA.
- Also on Thursday, February 15, two influenza-related reports appeared in the Morbidity and Mortality Weekly Report (MMWR): "Interim Estimates of 2017-18 Seasonal Influenza Vaccine Effectiveness – United States, February 2018" and "Update: Influenza Activity — United States, October 1, 2017–February 3, 2018"